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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/516,785	06/27/2005	Aladar A. Szalay	119356-00055 / 4804US	7336

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EXAMINER	
BURKHART, MICHAEL D	

ART UNIT	PAPER NUMBER
1633	

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04/01/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/516,785	SZALAY ET AL.	
	Examiner	Art Unit	
	MICHAEL BURKHART	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *7/28/2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,9,12-16,18 and 21-23* is/are pending in the application.

4a) Of the above claim(s) *3-5, 13 and 15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1, 2, 6, 9, 12, 16, 18, 22 and 23* is/are rejected.

7)☒ Claim(s) *14 and 16* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/29/08; 8/29/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt and entry of the amendment dated 7/28/2008 is acknowledged. After entry of the amendment, claims 1-6, 9, 12-16, 18, and 21-23 are pending. Claims 3-5, 13 and 15 remain withdrawn as directed to non-elected species.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Claim Rejections - 35 USC § 102

Claims 1, 2, 9, 12, 18 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Fu et al (1994, Zhonghua Wai Ke Za Zhi, cited by applicants). **This is a new rejection necessitated by amendment of the claims to recite administration of a bacterium (as opposed to a microorganism or cell) and to recite that detection is "within" the subject.**

Fu et al teach that bacterial flora of the gut can contaminate cutaneous burn wounds, by the detection of labeled *E. coli* in the burn wound (Abstract, page 2 of the English translation). The *E. coli* was recognized and cleared by the immune system, and thus is considered non-pathogenic (like most *E. coli*). See page 10, first full ¶ of the English translation. Fu teaches that one source of labeling was with the pUC19 plasmid, which encodes the antibiotic ampicillin (page 9 of the English translation), a therapeutic gene for wounded tissue that causes bacterial cell death. Fu et al teach that living bacteria were found to have reached the burn tissue after traveling through the stomach, lining of the gut, and the liver, hence, the E. coli are considered to replicate in the subject (again, like most *E. coli*, which, absent evidence to the contrary, are part

of the natural flora of the subject, in this case, rats). Because ampicillin was expressed, the E. coli are considered to comprise an inducible promoter regulating expression of ampicillin, that is, expression of ampicillin from the pUC19 vector is inducible upon introduction of the vector into a bacterial cell (the instant specification provides no limiting definition of an inducible promoter). Regarding claim 22, some subjects were treated with ampicillin (a therapeutic agent), see page 3 of the English translation.

Claims 1, 9 and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Hamblin et al. (2001, of record). **This rejection is maintained for reasons made of record in the Office Action dated 1/28/2008, and for reasons set forth below. Claim 23 has been added to this rejection due to amendment of the claim.**

Regarding claim 23, Hamblin et al teach administration of the bacterium into the wounds, (¶ linking pages 52 - 53). This is considered subcutaneous, topical, or intradermal administration.

Response to Arguments

Applicant's arguments filed 7/28/2008 have been fully considered but they are not persuasive. Applicants essentially assert that: 1) Hamblin et al do not disclose detection of a wound within a mouse; 2) Hamblin does not disclose detection of a wound because the wound is visible, and the bacteria were administered directly to the wound; .

Regarding 1), Hamblin et al teach administration and detection in wounds with dimensions of at least 8 X 12.5 X 5mm (page 52, second column, last ¶), thus, the bacterium was administered and detected "within" the subject.

Regarding 2), in response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., detecting only invisible wounds, not administering bacteria directly to the wound) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Claim Rejections - 35 USC § 103

Claims 6 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fu et al (1994, Zhonghua Wai Ke Za Zhi, cited by applicants) in view of Welling et al (2000, Euro. J of Nuclear Med., cited by applicants) and Weissleder et al. (2001, of record).

This is a new rejection necessitated by amendment of the claims to recite administration of a bacterium (as opposed to a microorganism or cell) and to recite that detection is "within" the subject.

The teachings of Fu et al are as above and applied as before. Fu et al do not teach detection of bacteria using MRI.

Welling et al demonstrate detectable labeling of molecules for *in vivo* use in MRI methods.

Weissleder et al teaches that MRI imaging using proteins such as transferrin was known in the art as an alternative to optical imaging. Weissleder et al further teaches that MRI provides the advantages of high spatial resolution and the ability to extract more than one measurement

parameter at a given imaging session. Thus, one would be motivated to substitute the MR imaging as taught by Weissleder and Welling et al for the optical imaging used in the method Fu et al. Moreover, the Artisan would expect success, as Fu et al had demonstrated that bacteria of exogenous origin could colonize inflamed wounds, such as burns, and the Art had already fleshed out the other detection methods, such as MRI.

Given the high level of skill in the art evidenced by the highly technical nature of the cited publications and applicants arguments (pages 10-14 of the reply dated 7/28/2008), one of ordinary skill in the art would have a reasonable expectation of success in practicing the method using MRI because doing so would require only the substitution of a MRI detectable protein or molecule (e.g., transferrin) for the fluorescent molecule (or pUC19) used by Fu et al and the use of standard MRI technology.

In addition, In *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007), the Supreme Court particularly emphasized "the need for caution in granting a patent based on a combination of elements found in the prior art," (*Id.* At 1395) and discussed circumstances in which a patent might be determined to be obvious. Importantly, the Supreme Court reaffirmed principles based on it precedent that "[t]he combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results." (*Id.* At 1395.) In the instant case, the prior art differs from the claimed invention only in the substitution of one detection modality (i.e., optical imaging) for another modality known in the art (i.e., MRI). However, one of skill in the art could have substituted MRI for optical imaging and the result of the substitution would have predictably resulted in an effective method of locating labeled cells at an area of inflammation or wounding. Therefore, the claimed invention, as a

whole, would have been obvious to one of ordinary skill in the art at the time the invention was made.

Allowable Subject Matter

Claims 14 and 21 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MICHAEL BURKHART whose telephone number is (571)272-2915. The examiner can normally be reached on M-F 8AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael Burkhart/
Primary Examiner, Art Unit 1633